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EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
09/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/579,007	PANICALI ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *23-32 and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 33-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/11/06, 12/31/08, 7/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the restriction/election requirement received on 7/2/09 has been entered. Applicant's election with traverse of the subject matter of Group I and the species "mucin" is acknowledged. Claims 1-43 are currently pending.

Applicants traverse the grounds for restriction between the identified Groups and specifically Groups I and II by arguing that the claims share a special technical feature and that since both Groups I and II encompass vectors encoding two breast cancer associated antigens that there would be no undue burden in examining both of Groups I and II. In response, the restriction requirement mailed on 4/2/09 clearly pointed out that no single technical feature unites all the identified groups, see pages 2-3, and further that the technical features present in the various Groups, which include vectors encoding one or more breast cancer associated antigens and nucleic acid molecules encoding a Muc-1 fragment are not special technical features as such products were well known in the prior art, as was their use to induce immune responses, see for example Grosenbach et al. (IDS of5/11/06, ref C6), Zajac et al. (IDS of5/11/06, ref C4), and Scholl et al. (IDS of5/11/06, ref C3). It is further noted that the examination of any group in additional to Group I would indeed place an undue burden on the examiner because the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries), and the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph. As such, applicant's traversal is not found persuasive and the restriction requirement is deemed proper and made FINAL.

Applicant's traverses the election of species requirement for same reasons, that there would be no added burden to search all species together. This is not agreed as each tumor antigen is a separate and distinct protein/peptide such that search and consideration of all species together would place a serious examination burden on the examiner since each species requires a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries); the prior art applicable to one species would not likely be applicable to another, and the various species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph. Therefore the traversal is not persuasive and the election of species requirement is deemed proper and made FINAL.

Claims 23-32, and 41-43 are therefore withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/2/09. Claims 1-22, and 33-40 are currently under examination. Please note that examination of any generic or linking claim is limited to the elected invention and species as no generic or linking claim(s) has been found allowable. An action on the merits follows.

Information Disclosure Statement

The information disclosure statements (IDS) filed on 5/11/06, 12/31/08, and 7/2/09 meet the requirements of 37 CFR 1.97 and 1.98 and have been considered by the examiner. Initialed and signed copies of the 1449s are attached to this action.

Claim Objections

Claim 7 is objected to because of the following informalities: claim 7 depends on itself. Appropriate correction is required. Since it would appear that claim 7 should depend on claim 6, in the interests of compact prosecution, claim 7 has been interpreted as including the limitations of claim 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-14, and 33-40 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/34494 (2000), hereafter referred to as Schlom et al.

Schlom et al. teaches one or more recombinant poxvirus vectors which encode a tumor associated antigen such as MUC1 (mucin) or CEA, and multiple co-stimulatory molecules (Schlom et al., pages 5-7, 34-35, 52-53, 55-56, 61-64, 113-116, 121-123). In particular, Schlom et al. teaches recombinant poxvirus encoding the co-stimulatory molecules B7-1, ICAM-1, and LFA-1 (referred to as TRICOM), and a tumor associated antigen (Schlom et al., pages 5-7, 31-33, 49-51, 53-54, 57-60, 113-116, 121-123). Schlom et al. further teaches that the vectors can

encode more than one tumor associated antigen, and/or further encode a cytokine such as GM-CSF (Schlom et al., pages 5, 31-37). In addition, Schlom et al. teaches that the recombinant poxvirus can be an orthopox virus, vaccinia virus, vaccinia-Wyeth, MVA, NYVAC, fowlpox, or avipox (Schlom et al., pages 25-26, 49-65). Schlom et al. also teaches recombinant poxvirus comprising a specific MUC1 nucleotide sequence where the nucleotide sequence encodes a truncated MUC1 having 10 tandem repeats where the nucleotide sequence of the repeats has been altered to minimize homology while maintaining the amino acid sequence (Schlom et al., pages 60-61). Note that such alteration of a nucleotide codon sequence without alteration of the encoded amino acid relies on codon wobble such that the resulting sequence can be referred to as "wobbled". Schlom et al. further teaches that the recombinant poxvirus encoding a tumor antigen such as MUC1 and TRICOM can be used to treat tumors such as breast cancer tumors (Schlom et al., pages 35-37). In addition, Schlom et al. teaches the administration of more than one dose of the recombinant virus, or a prime and boost delivery method where a first vector is administered followed by a administration of a second vector, where the first and second vectors are different strains of poxvirus (Schlom et al., page 39). Schlom et al. also teaches human clinical trials involving the repeat administration of recombinant vaccinia encoding a tumor associated antigen and TRICOM (Schlom et al., pages 98-99).

In regards to claim 38, it is noted that the claim recites where the Muc-1 fragment comprises "about 6 tandem repeat units". As noted in the rejection of the claim under 35 U.S.C. 112, second paragraph, below, it is unclear what number of tandem repeats qualifies as "about 6". In the interests of compact prosecution, this phrase has been interpreted to include 10 tandem repeat units.

In regards to claim 30, please note that the claim recites administering SEQ ID NO:1 or a fragment or variant thereof. While Schlom et al. does not teach a MUC1 sequence identical to SEQ ID NO:1, Schlom et al. does teach a similar wobbled MUC1 sequence comprising 10 tandem repeats that appears to qualify as a "variant" of SEQ ID NO:1.

Thus, by teaching all the limitations of the claims as written, Schlom et al. anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/34494 (2000), hereafter referred to as Schlom et al., in view of WO 01/24832 (2001), hereafter referred to as Pecher.

Schlom et al. teaches one or more recombinant poxvirus vectors which encode a tumor associated antigen such as MUC1 (mucin) or CEA, and multiple co-stimulatory molecules (Schlom et al., pages 5-7, 34-35, 52-53, 55-56, 61-64, 113-116, 121-123). In particular, Schlom et al. teaches recombinant poxvirus encoding the co-stimulatory molecules B7-1, ICAM-1, and LFA-1 (referred to as TRICOM), and a tumor associated antigen (Schlom et al., pages 5-7, 31-33, 49-51, 53-54, 57-60, 113-116, 121-123). Schlom et al. further teaches that the vectors can encode more than one tumor associated antigen, and/or further encode a cytokine such as GM-CSF (Schlom et al., pages 5, 31-37). In addition, Schlom et al. teaches that the recombinant poxvirus can be an orthopox virus, vaccinia virus, vaccinia-Wyeth, MVA, NYVAC, fowlpox, or avipox (Schlom et al., pages 25-26, 49-65). Schlom et al. also teaches recombinant poxvirus comprising a specific MUC1 nucleotide sequence where the nucleotide sequence encodes a truncated MUC1 having 10 tandem repeats where the nucleotide sequence of the repeats has been altered to minimize homology while maintaining the amino acid sequence (Schlom et al., pages 60-61). Note that such alteration of a nucleotide codon sequence without alteration of the

encoded amino acid relies on codon wobble such that the resulting sequence can be referred to as "wobbled". Schlom et al. further teaches that the recombinant poxvirus encoding a tumor antigen such as MUC1 and TRICOM can be used to treat tumors such as breast cancer tumors (Schlom et al., pages 35-37). In addition, Schlom et al. teaches the administration of more than one dose of the recombinant virus, or a prime and boost delivery method where a first vector is administered followed by a administration of a second vector, where the first and second vectors are different strains of poxvirus (Schlom et al., page 39). Schlom et al. also teaches human clinical trials involving the repeat administration of recombinant vaccinia encoding a tumor associated antigen, CEA, and TRICOM (Schlom et al., pages 98-99).

Schlom et al., while teaching vectors encoding one or more target antigens in combination with TRICOM, does not specifically teach to make and use a poxvirus vector encoding both MUC1 and CEA to treat breast cancer. Pecher et al. supplements Schlom et al. by teaching the combined administration of vectors, including vaccinia virus vectors, encoding MUC1 and CEA to human patients for the treatment of tumors (Pecher et al. pages 4-6). Therefore, in view of the teachings of Schlom et al. to use poxvirus vectors encoding more than one target tumor associated antigen for the treatment of cancers including breast cancer, and the motivation provided by Pecher to co-administer vaccinia virus encoding MUC1 and CEA to treat human tumors, it would have been *prima facie* obvious to the skilled artisan at the time of filing to make and use one or more poxviruses encoding MUC1, CEA, and TRICOM (B7, ICAM-1, and LFA-1) in the methods of treating cancer, such as breast cancer, taught by Schlom et al.. Further, based on the detailed guidance provided by Schlom et al. for making poxvirus vectors which encode multiple heterologous genes, and the successful demonstration by both Schlom et

al. and Pecher that poxvirus encoding tumor antigens such as CEA and MUC1 can successfully prevent tumor growth, the skilled artisan at the time of filing would have had a reasonable expectation of success in treating breast cancer using the methods of Schlom et al. as modified by Pecher et al.

Claims 1, 6-7, 11, and 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/34494 (2000), hereafter referred to as Schlom et al. in view of Grosenbach et al. (2001) Cancer Research, Vol. 61, 4497-4505.

Schlom et al. teaches one or more recombinant poxvirus vectors which encode a tumor associated antigen such as MUC1 (mucin) or CEA, and multiple co-stimulatory molecules (Schlom et al., pages 5-7, 34-35, 52-53, 55-56, 61-64, 113-116, 121-123). In particular, Schlom et al. teaches recombinant poxvirus encoding the co-stimulatory molecules B7-1, ICAM-1, and LFA-1 (referred to as TRICOM), and a tumor associated antigen (Schlom et al., pages 5-7, 31-33, 49-51, 53-54, 57-60, 113-116, 121-123). Schlom et al. further teaches that the vectors can encode more than one tumor associated antigen, and/or further encode a cytokine such as GM-CSF (Schlom et al., pages 5, 31-37). In addition, Schlom et al. teaches that the recombinant poxvirus can be an orthopox virus, vaccinia virus, vaccinia-Wyeth, MVA, NYVAC, fowlpox, or avipox (Schlom et al., pages 25-26, 49-65). Schlom et al. also teaches recombinant poxvirus comprising a specific MUC1 nucleotide sequence where the nucleotide sequence encodes a truncated MUC1 having 10 tandem repeats where the nucleotide sequence of the repeats has been altered to minimize homology while maintaining the amino acid sequence (Schlom et al., pages 60-61). Note that such alteration of a nucleotide codon sequence without alteration of the

encoded amino acid relies on codon wobble such that the resulting sequence can be referred to as "wobbled". Schlom et al. further teaches that the recombinant poxvirus encoding a tumor antigen such as MUC1 and TRICOM can be used to treat tumors such as breast cancer tumors (Schlom et al., pages 35-37). In addition, Schlom et al. teaches the administration of more than one dose of the recombinant virus, or a prime and boost delivery method where a first vector is administered followed by a administration of a second vector, where the first and second vectors are different strains of poxvirus (Schlom et al., page 39). Schlom et al. also teaches human clinical trials involving the repeat administration of recombinant vaccinia encoding a tumor associated antigen and TRICOM (Schlom et al., pages 98-99).

Although Schlom et al. teaches the administration of more than one dose of the recombinant virus, or a prime and boost delivery method where a first vector is administered followed by a administration of a second vector, where the first and second vectors are different strains of poxvirus, Schlom et al. does not specifically teach where 1-3 doses of an orthopox, such as vaccinia, NYVAC, or MVA, and multiple administration of an avipox are administered to the patient. Grosenbach et al. supplements Schlom et al. by teaching a vaccine strategy for administering poxvirus encoding tumor associated antigen and TRICOM that synergistically amplifies tumor antigen specific immune responses. Specifically, Grosenbach et al. teaches that a prime/boost strategy where a orthopox vaccinia virus encoding CEA and TRICOM is administered once followed by three boosts of a fowlpox encoding CEA and TRICOM substantially enhances tumor antigen specific immune responses (Grosenbach et al., pages 4501-4503).

Therefore, in view of the teachings of Schlom et al. to administer different strains of poxvirus encoding a tumor associated antigen such as MUC1 or CEA and TRICOM in a prime boost strategy, and the particular motivation provided by Grosenbach et al. to prime using one dose of vaccinia encoding a tumor antigen and TRICOM and boost with multiple doses of a fowlpox encoding a tumor antigen and TRICOM, it would have been *prima facie* obvious to the skilled artisan at the time of filing to administer a priming dose of an orthopox such as vaccinia, or other well known modified vaccinia such as NYVAC or MVA as taught by Schlom, encoding MUC1 and TRICOM followed by boosting with multiple doses of fowlpox encoding MUC1 and TRICOM to a patient at risk for or having a breast tumor with a reasonable expectation of success in preventing or delaying tumor growth. It is further noted that while Schlom et al. generally teaches repeat administrations of poxvirus and does not identify any particular interval between boosts of poxvirus, and Grosenbach et al. only specifically discloses repeat administrations of fowlpox at 1 or 2 week intervals, the normal desire of the artisan to improve upon what is already known would render the administration of boosts at for example 3 week intervals obvious. The applicant is reminded that "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 35 -38 recite various ranges for the number of Muc-1 tandem repeat units that are present in the Muc-1 fragment. However, as each of these claims utilizes the term "about", the metes and bounds of the number of Muc-1 tandem repeat units that can be present in the Muc-1 fragments for each of these claims cannot be determined. The term “about” is indefinite in that in the absence of a specific definition of the amount of variation encompassed by this modifier, it is unclear whether for example 13 or 15 tandem repeat units are encompassed by the phrase “about 6 to about 12 Muc-1 tandem repeat units”, or whether the phrase “about 6” encompasses 10 units, 8 units, or 5 units.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner’s supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner’s direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633